Hemodynamic
Changes in Hypertension

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DESPITE a vast amount of work devoted to the subject the nature of the fundamental hemodynamic changes in chronic, human hypertension is poorly understood. In this necessarily brief discussion the main outlines of the problem will be sketched in emphasizing the respective roles of the heart, large arteries and resistance vessels. Other factors such as the sympathetic nervous system, the baroreceptors and sodium ion will be briefly mentioned.

THE HEART

Cardiac Compensation and Decompensation

According to the Starling concept, an abrupt increase in arterial resistance will cause a temporary reduction in left ventricular output. The resulting retention of excess blood volume within the ventricle produces stretching of the myocardial fibers. According to Starling's "law," the energy of contraction is related directly to the length of the myocardial fibers in diastole. Thus, as a result of stretching of the fibers, the energy of myocardial contraction increases sufficiently to restore a normal cardiac output in the face of the increased arterial resistance. The retention of excess blood leads to left ventricular dilatation. This is the type of compensation seen in animal experiments where the peripheral resistance is increased suddenly, as by constricting the thoracic aorta.

Left ventricular hypertrophy is probably the most important compensatory mechanism for maintaining a normal cardiac output in the face of the increased peripheral arterial resistance seen in chronic hypertension. As opposed to animal experiments in which acute elevations of arterial pressure are imposed on a heart adjusted to a normal peripheral resistance, chronic hypertension in man is characterized by considerable

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left ventricular hypertrophy. The tension which the myocardium is capable of developing is, in general, proportional to the cross sectional area of the myocardial wall. Such a ventricle is a more powerful pump than a normal ventricle. When chronic as opposed to acute hypertension is produced in animals, it has been observed that the cardiac reserve is as great as in the normotensive animal.

There is no strict correlation between the height of the blood pressure and the point at which cardiac decompensation occurs when an exercise load is imposed. Some other factors in addition to the elevation of blood pressure appear to be involved in the development of congestive heart failure. Aside from such an obvious influence as coronary artery disease, these other factors are unknown. There is no doubt, however, that hypertension places an additional burden on the heart and contributes importantly to the development of heart failure. Reduction of the elevated blood pressure in decompensated patients can reverse the hemodynamic pattern of cardiac failure. Cardiac work is increased in hypertension and the oxygen requirement of the heart is elevated. Since the heart empties in systole the *mean* systolic pressure is a more important determinant of the cardiac load than is either diastolic or mean arterial pressure.

Cardiogenic Hypertension

Adrenergic substances such as epinephrine or norepinephrine and stimulation of the sympathetic nerves to the heart increase considerably the force of myocardial contraction. Stimulation of the left stellate ganglion not only raises the arterial systolic and pulse pressures but also the diastolic pressure. The reason for an increase in diastolic pressure when only the heart is stimulated is unknown. The diastolic elevation suggests some sort of interaction between the heart and the arterioles. Catecholamines are released from the myocardium into the circulation during sympathetic stimulation but the amounts are thought to be insufficient to produce hypertension. There is some evidence to suggest that an increase in pressure within arterioles stimulates contraction of their smooth muscle, the so-called "myogenic response." In any event the possibility has not been ruled out that some cases of hypertension may originate with an increase in the contractility of the left ventricle.

The critical factor may be the pressure developed within the ventricle rather than the output. Of interest in this connection are the observations made on pulmonary arterial pressures in patients with interatrial as compared to those with interventricular septal defects. Both anomalies are associated with increases in cardiac output. However, at comparable cardiac outputs, patients with interventricular septal defects exhibit far higher pulmonary arterial pressures than is the case in patients with interatrial septal defects. The difference appears to be due to the fact that in patients with interventricular septal defects the pulmonary artery is exposed to the higher pressures generated in the left ventricle. There is,

however, little direct evidence that myocardial "contractility" in human hypertension is abnormally influenced by neurogenic or hormonal factors. The most pertinent evidence has been the observation that the cardiac output is increased while the total peripheral resistance is normal in some patients with hypertension, particularly in juvenile hypertension. However, such results may be due to the apprehension of the patients during the procedure.

THE AORTA AND LARGE ARTERIES

The distensibility of the aorta to some extent cushions the impact of the systolic ejection and so decreases the height of systolic arterial pressure. Vasoconstrictor drugs reduce the distensibility of the aorta which contributes to the elevation of systolic pressure produced by these agents. Stiffening associated with the aging process and atherosclerosis of the aorta and other large arteries in elderly people often results in systolic hypertension. Elevation of pulse pressure also is commonly associated with essential hypertension in other age groups. The increased pulse pressure often seen in younger patients apparently is due to loss of aortic distensibility caused by the stretching and gradual distention of the aorta which occurs during long continued hypertension.

Coarctation of the Aorta

Coarctation of the aorta represents an experiment of nature of considerable hemodynamic interest. Studies in such patients indicate that the peripheral resistance is adjusted so as to provide a normal blood flow to all organs above and below the coarctation. For example, the peripheral vascular resistances appear to be normal in the renal, hepatic and calf segment vascular beds in contrast to essential hypertension where they are elevated. On the other hand the vascular resistance is elevated in the forearm. It appears that the body can adjust vascular tone differently above and below the coarctation so as to meet the requirements of the various tissues for a normal blood flow. The mechanism by which this is brought about is not known.

The resting cardiac output often is elevated in coarctation of the aorta and this together with the decrease in aortic capacity accounts for the large pulse pressure found in arteries above the coarctation. The systolic pressure increases alarmingly with exercise when it may exceed 300 mm. Hg. These severe elevations probably contribute to the aortic damage leading to dissecting aneurysm of the aorta commonly seen in this condition. The height to which the blood pressure rises during exercise provides an indication of the degree of constriction of the aorta. Abnormal elevations of pulmonary wedge pressures also occur during physical exertion. These various abnormal responses to exercise are reversed following successful aortic reconstruction.

THE ARTERIOLES

The Peripheral Resistance

Arterial pressure may rise either from an elevation of cardiac output or an increase in the resistance of the peripheral vessels to the outflow of blood from the arteries. In the majority of patients with established hypertension the peripheral resistance is increased and the cardiac output is normal until such time as heart failure supervenes. The increased resistance is due primarily to arteriolar constriction although there is some evidence to suggest that the capillaries may be narrowed, elongated and sparsely distributed. The peripheral resistance is increased generally all over the body being highest in the kidneys and, according to some reports, somewhat less elevated in voluntary muscles than in other areas.

Factors Influencing Arteriolar Tone

Many influences can affect the state of contraction of arteriolar smooth muscle. Local changes in the environment of a given arteriole can influence its calibre. A decrease in tissue oxygen concentration or an increase in carbon dioxide concentration produces relaxation of arteriolar smooth muscle. There is some evidence to suggest that increases in intraluminal pressure cause a "myogenic response" which results in arteriolar constriction. Alterations of the relative concentrations of sodium and potassium inside, as compared to outside the cells, influence the contractility of smooth muscle. The importance of these various factors in producing the increased peripheral resistance seen in hypertension is not known.

In addition to these local factors, the peripheral vessels can be influenced by the sympathetic nervous system. Stimulation of the sympathetic nerves results in a complex cardiovascular response in which blood flow is redistributed from the abdominal viscera and skin to the voluntary muscles. Fear and apprehension activate these responses. In the response to emotional stress cardiac output may increase or remain essentially unchanged. Some investigators but not all have found a trend toward increased blood flow in the forearm segment of patients with essential hypertension. This observation along with the frequent decrease in renal blood flow has been compared to the pattern of response seen with emotional stress. It has been cited as evidence for increased activity of the sympathetic nervous system in the pathogenesis of essential hypertension.

If the sympathetic nervous system accounts for the increased arteriolar constriction, one would expect a greater than normal relaxation of these arterioles after they have been released from sympathetic stimulation. The result would be an increase in blood flow to the denervated part. However, blood flow changes following sympathetic block or denervation of various body areas are essentially the same in hypertensive and

normotensive individuals. The evidence for a neurogenic etiology of hypertension, therefore, is conflicting.

There is evidence to indicate that the autonomic nervous system contributes to the maintenance of the hypertension once it has been established through other mechanisms. For example, it has been demonstrated in dogs with experimental renal hypertension that the baroreceptor nerves of the carotid sinus readjust to the higher level of pressure. Whereas, prior to the hypertension the carotid sinus nerves responded to distending pressures slightly exceeding normal arterial pressure, after the establishment of renal hypertension they did not respond until the sinus pressure had been raised to considerably higher values, that is, above the existing hypertensive level of arterial pressure. Similarly, in these hypertensive animals, reducing the intrasinus pressure toward normal evoked reflex vasoconstriction. It appears, therefore, that the baroreceptor nerves can be "reset" to recognize a long-continued elevation of blood pressure as normal thereby providing an additional mechanism for the maintenance of the hypertension.

SODIUM IN HYPERTENSION

It is well known that diets severely restricted in salt content or the administration of saluretic agents often reduce the blood pressure of hypertensive patients. In addition, reactivity to pressor influences is reduced and responsiveness to depressor agents is increased. Depletion of sodium ion appears to be the important element in these responses. At least part of the initial antihypertensive effect of saluretic agents is due to reduction in plasma volume. Diets very low in sodium also may deplete the extracellular fluid and plasma volumes. However, after long-term administration of chlorothiazide the plasma and extracellular fluid volumes return toward pretreatment levels although the blood pressure remains reduced. Some other factor, the nature of which is not understood, is involved in maintaining the reduction of arterial pressure.

According to some investigators the sodium content of the walls of large arteries and aorta is increased in experimental hypertension while according to others it is not. It has been proposed that in hypertension the arteriolar walls are "waterlogged," resulting in narrowing of the arteriolar lumina. Because of their small size, however, it has not been possible to test this hypothesis by direct measurement. Increasing the sodium concentration in the blood decreases arteriolar resistance and produces systemic hypotension. Similarly, increasing the sodium content in the fluid bathing isolated smooth muscle strips decreases their tension. Hypotonic sodium solutions are said to have the opposite effect. Changes in potassium content also influence the tension of arterial strips. These various observations illustrate the complexity of the relationships between sodium ion and vascular tone. There is no direct evidence at the

present time to indicate that the sodium content of the arterioles is abnormal in patients with hypertension.

EXAGGERATED NATRIURESIS

When intravenous infusions are administered to hypertensive patients they respond by excreting sodium chloride and water at a higher rate than normal in the urine. This exaggerated natriuresis can be reduced toward normal by lowering the blood pressure with antihypertensive agents or by sympathectomy and may be abolished by pretreatment with a low sodium diet. On the other hand, further elevation of blood pressure with angiotensin increases sodium excretion in hypertensive patients but not in normotensive subjects. These observations point toward a disturbance in the excretion of salt and water in hypertension the origin of which remains obscure. Exaggerated natriuresis does not seem to be related to changes in glomerular filtration rate or renal plasma flow or to renal tubular damage, but rather to decreased renal tubular reabsorption of salt and water. Under basal conditions in hypertensive patients the excretion of these substances is normal and appears only when intravenous infusions or angiotensin are administered.

SUMMARY

Left ventricular work and oxygen requirements are increased in hypertension. Since the heart contracts against the systolic pressure head it is the mean systolic rather than the diastolic pressure which determines the resistance load on the ventricle. In acute hypertension the left ventricle compensates for the increased peripheral vascular resistance by dilatation (increase in diastolic fiber length), but in chronic hypertension the principal mechanism for compensation is hypertrophy (increase in cross-sectional area of contractile elements). The interesting possibility has not been ruled out that some instances of hypertension could result from an increase in the energy of myocardial contraction.

The aorta and large arteries become less distensible in chronic hypertension probably as a result of stretching and early degenerative changes resulting in an increase in pulse pressure. The hemodynamic adjustments in coarctation of the aorta are remarkable in that the peripheral vascular resistance appears to be adjusted differently above and below the aortic constriction. It is lower below the coarctation, thus providing a normal distribution of blood flow throughout the body.

The principal site of the increased vascular resistance is in the arterioles but the postarteriolar small vessels also may share in the vasoconstrictor response. Little is known about factors that control the basal tone of vascular smooth muscle. It has not been possible to determine the importance of local oxygen and carbon dioxide tensions, intraluminal

pressures or sodium and potassium concentrations in the pathogenesis of hypertension. The evidence for an increase in the activity of the sympathetic nervous system in essential hypertension is conflicting, most observations suggesting that sympathetic tone is normal. However, the baroreceptor nerves are easily reset to combat deviations of blood pressure from the existing hypertensive level.

Sodium depletion lowers blood pressure and alters pressor responsiveness in hypertensive patients. This is due in part to a fall in plasma volume and in part to unknown factors. Although there are some observations indicating an increase in the cation and water content of large arteries in experimental hypertension, evidence for similar changes occurring in the arterioles is entirely lacking. Hypertensive patients respond to intravenous infusions with exaggerated natriuresis. The natriuresis can be reduced by administering antihypertensive agents or by pretreatment with a sodium-restricted diet. The mechanism of the exaggerated natriuresis is unknown.

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